REMARKS

FORMAL MATTERS:

Claims 29 and 42 and 44-56 are pending and stand rejected.

In view of the remarks set forth below, reconsideration of this application is respectfully requested.

OBJECTIONS

The amendment filed on October 30, 2007 is objected to under 35 U.S.C. § 132(a) because it allegedly introduces new matter into the disclosure. Specifically, the Examiner believes the added material is new matter because support for the added material was allegedly not provided.

This objection is respectfully traversed on the basis that support for the added material is explicitly provided in the second paragraph of page 6 of the Applicant's prior response, reproduced below for the Examiner's convenience:

> line 7 of page 49, Fig. 2. Support for the amendment to the specification is found in lines 9 to 23 of page 28 of provisional application serial no. 60/282,356, which application is incorporated by reference in the first paragraph of the instant application.

Since the added material is found in lines 9-23 of page 28 of provisional application serial no. 60/282,356, which application is incorporated by reference in the first paragraph of the instant application, this objection is believed to be moot and may be withdrawn.

Withdrawal of this objection is respectfully requested.

REJECTION UNDER §101

Claims 29 and 42 and 44-56 stand rejected under 35 U.S.C. § 101 as lacking patentable utility. The Applicants respectfully traverse this rejection.

The Applicants initially note that this Office Action appears to present several distinct lines of argument in over 30 pages of text. Since this case is being prepared for appeal, the Examiner is kindly requested to distill his arguments so that they can be more readily addressed by the Applicants.

Further, the Applicants note that in many places in the Office Action the Examiner has characterized the Applicants' arguments inappropriately. For example, the Examiner states: "In conclusion applicant is arguing that since hRUP35 is expressed in specific regions of the brain, it is involved or linked to motor control". (OA, p. 4), "Therefore applicant cannot use post-filing art to assert utility on their claimed invention" (OA, p.6), and "All applicants' arguments are based on it being expressed in the thalamus" (OA, p. 12). For the record, the Applicants do not agree with the Examiner's mis-characterizations of the Applicants arguments.

As best understood from the Office Action, the Applicants understand that this rejection is based on the following arguments: 1) the asserted utility is not adequately specific; 2) the asserted utility requires identification of a ligand; and 3) the asserted utility is based on homology to known GPCRs. These arguments are addressed in separate sections below. If the Examiner deems that not all arguments have been addressed, the Examiner is kindly requested to point out which arguments have not been addressed so that they can be addressed in appeal.

Assertion of Utility in Motor Control is Adequately Specific

The bulk of the Office Action (particularly page 5 to page 19) is focused on whether the asserted role of hRUP35 in motor control is adequately specific to meet the utility requirement of § 101.

The instant specification unequivocally states that hRUP35 is involved in motor control.[1] At the filing date of the instant application, therefore, the utility for hRUP35 in motor control was known to the Applicants, and asserted in the instant application. After the filing date of the instant application, statements supporting hRUP35's role in motor control were independently

[1] See, e.g., page 19, lines 9-11 of the instant specification: "For example and not limitation, proteins located/expressed in areas of the thalamus [e.g., hRUP35] are associated with sensorimotor processing and arousal" and the last paragraph of the prior amendment to the instant specification: "RUP35 was specifically expressed in the thalamus of the brain, suggesting that RUP35 may play a role in sensorimotor processing and arousal". Text in brackets added by Applicants.

made by *Susens*.[2] Subsequently, hRUP35's role in motor control was independently confirmed by *Torres*[3] using knockout mice.

Notwithstanding the asserted utility in motor control, the Examiner repeatedly argues that the asserted role of hRUP35 in motor control is inadequately specific. Specifically, the Examiner states that "Applicants have asserted that hRUP35 is linked to motor control but have not identified a specific motor function it is involved in" (OA, p.5), "there is no disclosure of the specific association with a specific motor function" (OA p.9), "what is the specific disorder or dysfunction that is specifically associated with claimed hRUP35" (OA p.10), and "It noted that neither the specific activity of GPCR or SEQ ID NO:16 or the specific treatable disease associated with the GPCR of SEQ ID NO:16 is disclosed". Similar statements are made throughout this rejection.

However, the Examiner does not cite any authority for the implicit contention that such details are required by the USPTO in order to establish a specific utility for a claimed invention. While disclosure of a specific disease correlation may be used by an Applicant to support an assertion of utility, the Examiner is going beyond the dictates of the law in requiring the Applicants to cite such disclosure in order to establish the utility of the claimed invention. In fact, the Examiner is not contending that the application lacks an asserted utility. Rather, he is just contending that the asserted utility is too broad and encompasses symptoms of different diseases and is not, therefore, specific enough to satisfy the requirements of §101. Again, Applicants cannot find any authority in the law for such a rejection.

Moreover, according to the MPEP 2107.01, citing *In re Fisher*[4], it is important for Office personnel to distinguish between *general* and *specific* utilities. According to *In re Fischer*,

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[2] See, e.g., page 520, last sentence, of *Susens* (Neuropharmacology 2006 50:512-520), where *Susens* states "The presence of GPR139 [which is the same as hRUP35] in brain areas involved in motor control suggests a function as mediator in locomotor activity." This reference was cited by the Examiner in the Office Action mailed September 12, 2006, as reference U. Text in brackets added by Applicants.

[3] See, e.g., *Torres et al.*, Abstract 328 of the 2006 Keystone Symposium. The Torres abstract reports that mutant mice lacking the mouse homolog of hRUP35 display a motor deficit. *Torres* was cited in a supplemental IDS in June 21 2006 as references AC.

[4] *In re Fisher*, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005)

general utilities are applicable to the broad class in which an invention belongs. For example, general utilities for a biopolymer include, for example, "as a probe to isolate other polynucleotides", "to make antibodies" or "as a marker to make a genetic map". The Applicants are not arguing that hRUP35 has a general utility. Rather, the Applicants argue that hRUP35 is specifically involved in motor control. *The asserted utility of hRUP35 is not applicable to all GPCRs* and is, therefore, not a general utility.

The Applicants respectfully submit that the claimed polynucleotide should be treated no differently than other patentable polynucleotides that can be used, for example, to identify drugs for the treatment of symptoms, e.g., inflammation and pain, that are associated with a number of diseases.

The Examiner's requirement that the Applicants point out specifically a particular disease to which hRUP35 is linked is a mis-interpretation of the law.

Summarizing the foregoing discussion, the Applicants believe the Examiner's rejection is based on a standard that is much higher than that required for satisfying 35 U.S.C. § 101. Thus, this rejection should be withdrawn.

The Applicants believe that the main thrust of the Office Action has been addressed above. To the extent that further discussion is necessary, other allegations asserted in the Office Action are discussed below.

Applicant's Assertion of Utility is Not Based on Homology to Known GPCRs

In the Office Action, the Examiner argues over approximately nine pages that protein function is difficult to predict by sequence alone (OA pp. 20–28). Specifically, the Examiner argues that "the unpredictability of assigning a function to a particular protein based on homology, especially one that belongs to the family of GPCRs, which have very different ligand specificity and functions." (OA, p. 27

However, Applicants do not believe that they have ever attempted to assert utility for hRUP35 based solely on homology to known GPCRs. If the Examiner disagrees, Applicants respectfully request that the Examiner identify where in the prosecution such assertions were made by Applicants. In the absence of such identification and in order to simplify ongoing

prosecution, Applicants respectfully request that the Examiner withdraw these arguments as inapplicable.

Assertion of Utility Does Not Require Identification of a Ligand

The Examiner additionally states that the receptor has "no known ligand or known function" and "it is unpredictable what ligands will bind to orphan receptors, and further the functional effects of ligand may remain uncertain after extensive experimentation" (OA, p.19 check this) However, the Examiner does not cite any authority for the implicit contention that identification of a ligand is required by the USPTO in order to establish a specific utility for a claimed invention. While disclosure of a ligand may be used by an Applicant to support an assertion of utility, the Examiner is going beyond the dictates of the USPTO Guidelines in requiring the Applicants to cite such disclosure in order to establish the utility of the claimed invention. This is particularly true in the instant situation where the Applicants have shown that the receptor is active in the absence of ligand. Applicants respectfully request that the Examiner identify on what authority identification of a ligand is required by the USPTO in order to establish a specific utility for a claimed invention. Absent such authority, Applicants respectfully request that the Examiner reconsider and withdraw arguments based on identification of a ligand.

Post-Filing Art is Not Relevant in Determining "Skill in the Art" at Time of Filing

The Examiner cites also scientific literature to question such matters as the cells used in the instant application and the conclusions drawn therefrom. (i.e., OA, pp.13-14). The Examiner concludes from this literature that a skilled artisan would believe further research was required in order to make Applicants' asserted utility credible. (Id.). However, in making these arguments, the Examiner cites many documents published after the filing date of Applicants' invention. Without addressing the merits of these arguments, Applicants believe that such hindsight analysis is completely inappropriate for a utility analysis and has no basis in the USPTO Guidelines. If the Examiner desires to discuss the "skilled artisan" or the thinking of one of skill in the art, such discussion should center on one of skill in the art at the time the application was filed. Applicants respectfully request that the Examiner identify on what

authority post-filing documents may be utilized as a basis for establishing the skill of one of the art at the time of filing. Absent such authority, Applicants respectfully request that the Examiner reconsider and withdraw arguments based on post-filing art.

The Examiner Has Not Met the Burden for a *Prima Facie* Showing

To overcome the presumption of sufficient utility as asserted by the Applicant, the Examiner must carry the initial burden to make a *prima facie* showing of lack of utility and provide evidentiary basis for the conclusion. In other words, the Examiner "must do more than merely question operability – [he] must set forth factual reasons which would lead one skilled in the art to question the objection truth of the statement of operability". *In re Gaubert*, 187 USPQ 664, 666 (CCPA, 1975).

In the present case, the Applicants have asserted in the instant specification that hRUP35 (which is encoded by the claimed polynucleotides) is involved in motor control, and thus has a substantial and real-world utility, for example, in identifying compounds that can be used to treat sensorimotor processing-related disorders. *Susens* and *Torres*, which are both of record, confirm that the asserted utility is credible.

In contrast, the Examiner has not provided any specific evidence or objective reason to question the objective truth of the Applicants' statements about the role of hRUP35 in motor control. In other words, in citing *Susens* and *Torres*, the Applicants have provided substantial evidence confirming hRUP35's asserted utility in motor control, and the Examiner has provided no specific evidence to contradict the Applicants' statements. Thus, the Applicants believe that the Examiner has not met the burden of making a *prima facie* showing of lack of utility. As such, this rejection should be withdrawn.

Since the Examiner has provided no evidence to support this rejection, the Examiner is again requested, under MPEP § 2144.03[5], to provide an affidavit of personal knowledge as to

[5] MPEP § 2144.03: "If the examiner is relying on personal knowledge to support the finding of what is known in the art, the examiner must provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. See 37 CFR 1.104(d)(2)".

why the person of ordinary skill would have reason to doubt the utility that is asserted in this case.

The Applicants' prior arguments still stand and are incorporated herein but not reiterated for the sake of brevity. In the event that the above arguments are found unpersuasive, the Applicants' prior arguments are hereby preserved for Appeal.

The Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

REJECTIONS UNDER §112, ¶1 (ENABLEMENT - UTILITY)

Claims 29 and 41-46 are rejected as not meeting the "how to use" part of the enablement requirement of 35 U.S.C. § 112, first paragraph.

The basis for this rejection is the Examiner's contention that the claims are not supported by a patentable utility.

As such, it is believed that this rejection has been adequately addressed in the discussion in the preceding section of this response.

In view of the discussion in the preceding section of this response, this rejection should be withdrawn.

REJECTIONS UNDER §112, ¶1 (WRITTEN DESCRIPTION)

Claims 44-56 are rejected as not meeting the written description requirements of 35 U.S.C. § 112, first paragraph. This rejection is respectfully traversed.

The rejected claims are directed to an isolated polynucleotide that encode a constitutively active PCR that is either at least 90% identical to SEQ ID NO:16 (e.g., claim 44) or at least 95% identical to SEQ ID NO:16 (e.g., claim 45).

The basis of this rejection is the Examiner's assertion that one of ordinary skill in the art of receptor biology would not be able to envision constitutively active G-protein coupled receptors comprising an amino acid sequence that is at least 90% or 90% identical to SEQ ID NO:

16. The basis for these rejections relates in large part to the claims encompassing variants of the human hARE35 protein that is explicitly disclosed in the specification.

The Applicants initially note that the claims are directed to an isolated polynucleotide encoding a GPCR which, as is well known and described in the instant specification, is a receptor containing seven transmembrane regions that is capable of transducing signals from the outside of a mammalian cell the inside of the cell. As such, the Applicants believe the claims recite only isolated polynucleotides that encode active GPCRs. Moreover, as shown in Fig. 2 and discussed on page 7 lines 5-6 of the instant specification, wild type hRUP35 (SEQ ID NO:16) is constitutively active. As such, the amino acid sequence of hRUP35 does not need to be altered to produce a constitutively active GPCR.

The Applicants submit that the structure/function relationship of GPCRs is well known and, as such, one of skill in the art would be able to envision a large number of operable variants of hRUP35 (SEQ ID NO:16).

For a description of GPCRs, the Examiner is respectfully directed to: a) page 3, line 2 to page 4, line 15 of the instant specification, where the structure/function relationship of GPCRs is described in detail; and b) the sections starting on page 17, 19 and 20 where a variety of methods for assaying GPCRs (which can be used to test variant proteins) are described in detail.

Further, as shown in Exhibit A, a search of NCBI's PubMed database reveals that there are over 2240 journal articles, including 298 reviews, that have a publication date that precedes the priority date of the instant application (November 27, 2000) and contain the phrase "GPCR" OR "G protein-coupled receptor" in the abstract. Thus, at the priority date of the instant application, GPCR proteins were a subject of significant interest in the scientific community. The art in which the subject hRUP35 protein belongs was therefore highly developed at the priority date of the instant application. For example, at the priority date of the instant application one of skill in the art would have knowledge of the atomic coordinates of at least one GPCR (see, e.g., Exhibit B). At the time of filing, the structure/function relationship of many GPCRs had been investigated (see, e.g., Exhibits C-E), and several reviews on the structure/function relationship of GPCRs had been published (see, e.g., Exhibits F-K listed on Exhibit B).

In addition, at the time of filing, one of skill in the art would have been aware of several algorithms for predicting GPCR structure (see, e.g., Exhibits L and M), an algorithm for

predicting important residues in GPCRs (see, e.g., Exhibit N), and reviews on the engineering of GPCRs by domain swapping (see, e.g., Exhibits O and P).

Given the vast amount of available information on structure/function relationships in GPCR proteins in general, in combination with the structure/function information on hRUP35 in the instant specification, the Applicant submits that one of skill in the art would be able to envision a large number of operable variants of hRUP35, and be able to use those variants without undue experimentation.

The Applicant understands that the effect of amino acid and nucleotide substitutions cannot be predicted with absolute certainty. However, given the functional limitation inherent to the claims, the information in the instant specification and the deep general understanding of the structure and function of GPCR proteins, the Applicant submits that such molecules are more than adequately described.

In addition, the Examiner is respectfully referred to pages 37-42 of the recently promulgated Written Description Training Materials (see www.uspto.gov/web/menu/written.pdf). These training materials indicate that claims that recite a polypeptide having at least "85% amino acid sequence identity" to a disclosed polypeptide can meet the written description requirement, even if there is little knowledge about the structure/functional relationship of the polypeptide. Since there is an abundance of knowledge relating to the structure/function relationship of GPCRs, the Applicants submit that the instant claims, which recite "90% identity" and "95% identity" language, are more than adequately described.

The Applicant submits that this rejection has been adequately addressed. Withdrawal of this rejection is requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number AREN-021CIP.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: August 6, 2008

By: /James S. Keddie, Reg. No. 48,920/
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Enclosures: Exhibits A-P and IDS to cite the same.
Pages 37-42 of the recently promulgated Written Description Training Materials

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TABLE OF EXHIBITS

J. Missale et al, *Dopamine receptors: from structure to function*. Physiol Rev. 1998 78:189-225 (Review)

K. Sealfon et al, *Functional domains of the gonadotropin-releasing hormone receptor.* Cell Mol Neurobiol. 1995 15:25-42 (Review)

L. Filizola et al, *BUNDLE: a program for building the transmembrane domains of G-protein-coupled receptors*. J Comput Aided Mol Des. 1998 12:111-8.

M. Orry et al, *Modeling and docking the endothelin G-protein-coupled receptor*. Biophys J. 2000 79:3083-94.

N. Califano *SPLASH: structural pattern localization analysis by sequential histograms.*
Bioinformatics. 2000 16:341-57.

O. Gouldson et al, *Domain swapping in G-protein coupled receptor dimers.* Protein Eng. 1998 11:1181-93.

P. Gouldson et al, *Dimerization and domain swapping in G-protein-coupled receptors: a computational study*. Neuropsychopharmacology. 2000 23:S60-77.

09/995 225 Exhibit A

Limits: **Publication Date from 1980/01/01 to 2000/11/26**

1: Arvanitakis L, Geras-Raaka E, Gershengorn MC. Related Articles, Links

Constitutively signaling g-protein-coupled receptors and human disease.
Trends Endocrinol Metab. 1998 Jan-Feb;9(1):27-31.
PMID: 18406231 [PubMed - in process]

2: Milligan G. Related Articles, Links

New aspects of g-protein-coupled receptor signalling and regulation.
Trends Endocrinol Metab. 1998 Jan-Feb;9(1):13-9.
PMID: 18406229 [PubMed - in process]

3: Tomlinson B. Related Articles, Links

IUPHAR Southeast Asian-Western Pacific Region--eighth Meeting. Pharmacology in the Next Millennium. 1-5 November 1999, Taipei, Taiwan.
IDrugs. 2000 Feb;3(2):182-4.
PMID: 16107936 [PubMed]

4: Iaccarino G, Koch WJ. Related Articles, Links

Therapeutic potential of G-protein coupled receptor kinases in the heart.
Expert Opin Investig Drugs. 1999 May;8(5):545-54.
PMID: 15992114 [PubMed]

5: Gehlert DR, Hipskind PA. Related Articles, Links

Neuropeptide Y receptor antagonists in obesity.
Expert Opin Investig Drugs. 1997 Dec;6(12):1827-38.
PMID: 15989583 [PubMed]

6: Jasionowski M, Grzonka Z, Lankiewicz L. Related Articles, Links

[G protein-coupled receptors (GPCR), ligand-receptor interaction studies]
Postepy Biochem. 2000;46(1):60-72. Review. Polish. No abstract available.
PMID: 15971378 [PubMed - indexed for MEDLINE]

7: Mayor F Jr, Penela P, Ruiz-Gómez A. Related Articles, Links

Role of G protein-coupled receptor kinase 2 and arrestins in beta-adrenergic receptor internalization.
Trends Cardiovasc Med. 1998 Jul;8(5):234-40.
PMID: 14987570 [PubMed]

Example 11: Percent Identity

11A: Art-Recognized Structure-Function Correlation Not Present

Specification:

The specification discloses a polynucleotide having the nucleic acid sequence of SEQ ID NO: 1, which encodes the polypeptide of SEQ ID NO: 2. The polypeptide of SEQ ID NO: 2 has the novel activity X, and does not share significant sequence identity with any known polypeptide or polypeptide family. The specification does not disclose any nucleic acid sequences that encode a polypeptide with novel activity X other than SEQ ID NO: 1.

Claims:

Claim 1. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2.

Claim 2: An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity X.

Analysis:

Claim 1

Claim 1 encompasses nucleic acids that encode the polypeptide of SEQ ID NO: 2, as well as those that encode any polypeptide having 85% structural identity to SEQ ID NO: 2. However, the specification discloses only a single species that encodes SEQ ID NO: 2; *i.e.*, SEQ ID NO: 1. There are no other drawings or structural formulas disclosed that encode either SEQ ID NO: 2 or a sequence with 85% identity to SEQ ID NO: 2.

The recitation of a polypeptide with at least 85% identity represents a partial structure, that is, at least 85% percent of the amino acids in the polypeptide will match those in SEQ ID NO: 2, and up to 15% of them may vary from those in SEQ ID NO: 2. However, there is no teaching regarding which 15% of the amino acids may vary from SEQ ID NO: 2. Consequently, there is also no information given about which nucleotides will vary from SEQ ID NO: 1 in the claimed genus of nucleic acids.

There is no functional limitation on the nucleic acids of claim 1 other than that they encode the polypeptide of SEQ ID NO: 2 or any polypeptide having 85% structural identity to SEQ ID NO: 2. The genetic code and its redundancies were known in the art before the application was filed.

The disclosure of SEQ ID NO: 2 combined with the pre-existing knowledge in the art regarding the genetic code and its redundancies would have put one in possession of the ge-

nus of nucleic acids that encode SEQ ID NO: 2. With the aid of a computer, one of skill in the art could have identified all of the nucleic acids that encode a polypeptide with at least 85% sequence identity with SEQ ID NO: 2. Thus, one of ordinary skill in the art would conclude that the applicant was in possession of the claimed genus at the time the application was filed.

Conclusion:

The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the scope of claim 1.

Claim 2

Claim 2 encompasses nucleic acids that encode the polypeptide of SEQ ID NO: 2, and nucleic acids that encode a polypeptide having 85% sequence identity to SEQ ID NO: 2 and have activity X. The specification discloses the reduction to practice of only a single species that encodes SEQ ID NO: 2 and has activity X; *i.e.*, SEQ ID NO: 1. There are no other drawings or structural formulas disclosed of a nucleic acid that encodes either SEQ ID NO: 2 or a polypeptide having 85% sequence identity to SEQ ID NO: 2 and activity X.

The claim includes a genus that can be analyzed at several levels sequentially for the purpose of focusing the issue.

First, the disclosure of SEQ ID NO: 2 combined with pre-existing knowledge in the art regarding the genetic code and its redundancies would have put one in possession of the genus of nucleic acids that encode SEQ ID NO: 2. With the aid of a computer, one of skill in the art could identify all of the nucleic acid sequences that encode a polypeptide with at least 85% sequence identity with SEQ ID NO: 2. However, there is no teaching regarding which 15% of the amino acids can vary from SEQ ID NO: 2 and still result in a protein that retains activity X. Further, there is no disclosed or art-recognized correlation between any structure other than SEQ ID NO: 2 and novel activity X.

An important consideration is that structure is not necessarily a reliable indicator of function. In this example, there is no disclosure relating similarity of structure to conservation of function. General knowledge in the art included the knowledge that some amino acid varia-

TECHNICAL NOTE

For information on amino acid substitution exchange groups and empirical similarities between amino acid residues, see a standard text such as Schulz et al., PRINCIPLES OF PROTEIN STRUCTURE, pp. 14-16, Springer-Verlag (New York 1979). There is a limit to how much substitution can be tolerated before the original tertiary structure is lost. Generally, tertiary structure conservation would be lost when the amino acid sequence varies by more than 50%. See, e.g., Cyrus Chothia and Arthur M. Lesk, "The relation between the divergence of sequence and structure in proteins," 5 THE EMBO JOURNAL 823-26 (1986).

tions are tolerated without losing a protein's tertiary structure. The results of amino acid substitutions have been studied so extensively that amino acids are grouped in so-called "exchange groups" of similar properties because substituting within the exchange group is expected to conserve the overall structure. For example, the expectation from replacing leucine with isoleucine would be that the protein would likely retain its tertiary structure. On the other hand, when non-exchange group members are substituted, e.g., proline for tryptophan, the expectation would be that the substitution would not likely conserve the protein's tertiary structure. Given what is known in the art about the likely outcome of substitutions on structure, those in the art would have likely expected the applicant to have been in possession of a genus of proteins having a tertiary structure similar to SEQ ID NO: 2 although the claim is not so limited.

However, conservation of structure is not necessarily a surrogate for conservation of function. In this case, there is no disclosed correlation between structure and function. The need for correlating information can vary. More specifically, those of skill in the art might require more or less correlating information depending on the kind of protein activity. If activity X is simply structural, e.g., a member of the collagen class, correlating information might not be a critical factor. However, if activity X is enzymatic, and there is no disclosure of the active site amino acid residues responsible for the catalytic activity, lack of that kind of correlating information may be a problem. Similarly, if activity X is as a ligand, and there is no disclosure of the domain(s) responsible for the ligand activity, the absence of information may be persuasive that those of skill in the art would not take the disclosure as generic.

Summarizing, there are no known or disclosed proteins having activity X other than SEQ ID NO: 2. As of the filing date, there was no known or disclosed correlation between a structure other than SEQ ID NO: 2 and activity X. While general knowledge in the art may have allowed one of skill in the art to identify other proteins expected to have the same or similar tertiary structure, in this example there is no general knowledge in the art about activity X to suggest that general similarity of structure confers the activity. Accordingly, one of skill in the art would not accept the disclosure of SEQ ID NO: 2 as representative of other proteins having activity X.

Conclusion:

The specification, taken with the pre-existing knowledge in the art of amino acid substitution and the genetic code, fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the scope of claim 2.

11B: ART-RECOGNIZED STRUCTURE-FUNCTION CORRELATION PRESENT

Specification:

The specification discloses a polynucleotide having the nucleic acid sequence of SEQ ID NO: 1, which encodes the polypeptide of SEQ ID NO: 2. The polypeptide of SEQ ID NO: 2

has a novel activity Y, and does not share significant sequence identity with any known polypeptide or polypeptide family. The specification does not disclose any nucleic acid sequences that encode a polypeptide with novel activity Y other than SEQ ID NO: 1. However, the specification discloses data from deletion studies that identify two domains as critical to activity Y, *i.e.*, a binding domain and a catalytic domain. The specification proposes that conservative mutations in these domains (e.g., one basic amino acid substituted for another basic amino acid) will still result in a protein having activity Y, whereas most non-conservative mutations in these domains will not result in a polypeptide having the recited activity. The specification also proposes that most mutations, conservative or non-conservative, outside the two domains will not affect activity Y to any great extent.

Claims:

Claim 1. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2.

Claim 2. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity Y.

Analysis:

Claim 1

(This analysis proceeds the same as the analysis for claim 1 in Example 11A (Art-Recognized Structure-Function Correlation Not Present)

Claim 1 encompasses a vast genus of nucleic acids that encode the polypeptide of SEQ ID NO: 2, as well as those that encode any polypeptide having 85% structural identity to SEQ ID NO: 2.

The specification, however, discloses the reduction to practice of only a single species that encodes SEQ ID NO: 2, *i.e.*, SEQ ID NO: 1. There are no other drawings or structural formulas disclosed that encode either SEQ ID NO: 2, or a sequence with 85% identity to SEQ ID NO: 2.

Although the recitation of a polypeptide with at least 85% identity represents a partial structure -- in that 85% percent of the polypeptide is known, while 15% of the structure may vary -- there is no teaching regarding which 15% of the amino acids will vary from SEQ ID NO: 2. Consequently, there is also no information about which nucleotides will vary from SEQ ID NO: 1 in the claimed genus of nucleic acids.

There are no functional characteristics disclosed for the nucleic acids of claim 1 other than they encode the polypeptide of SEQ ID NO: 2 or any polypeptide having 85% structural identity to SEQ ID NO: 2. Further, the specification fails to disclose a method of making nucleic acids encoding polypeptides having 85% identity to SEQ ID NO: 2.

Nonetheless, the disclosure of SEQ ID NO: 2 combined with the knowledge in the art regarding the genetic code would put one in possession of the genus of nucleic acids that encode SEQ ID NO: 2. Further, with the aid of a computer, one could list all of the nucleic acid sequences that encode a polypeptide with at least 85% sequence identity with SEQ ID NO: 2. Additionally, the level of skill and knowledge in the art is such that one of ordinary skill would be able to use conventional sequencing and nucleic acid synthesis techniques to routinely generate and identify nucleic acids that encode the polypeptide of SEQ ID NO: 2, as well as those that encode any polypeptide having 85% structural identity to SEQ ID NO: 2. Thus, one of ordinary skill in the art conclude that the applicant would have been in possession of the claimed genus at the time of filing.

Conclusion:

The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the scope of claim 1.

Claim 2

Claim 2 encompasses a genus of nucleic acids that encode the polypeptide of SEQ ID NO: 2 and those that encode any polypeptide having 85% structural identity to SEQ ID NO: 2, wherein the polypeptide additionally has activity Y.

The specification, however, discloses the reduction to practice of only a single species that encodes SEQ ID NO: 2 and has activity Y, *i.e.*, SEQ ID NO: 1. There are no other drawings or structural formulas disclosed of a nucleic acid that encodes either (i) SEQ ID NO: 2 or (ii) a polypeptide with 85% sequence identity to SEQ ID NO: 2 wherein the polypeptide also has activity Y.

The disclosure of SEQ ID NO: 2 combined with the knowledge in the art regarding the genetic code would have put one in possession of the genus of nucleic acids that encode SEQ ID NO: 2. Further, with the aid of a computer, one could list all of the nucleic acid sequences that encode a polypeptide with at least 85% sequence identity to SEQ ID NO: 2. However, the specification fails to teach which of the nucleic acid sequences that encode a polypeptide with at least 85% sequence identity to SEQ ID NO: 2 encode a polypeptide having the required activity Y.

Nonetheless, the specification identifies two domains responsible for activity Y, *i.e.*, a binding domain and catalytic domain. The specification also predicts that conservative mutations in these domains will result in a protein having activity Y. Although all conservative amino acid substitutions in these domains will not nec-

Practice Note

This example deals only with the written description analysis of the claimed nucleic acids. Enablement issues that may be raised by the recited facts are not addressed here, but should be considered during examination. A separate rejection for nonenablement should be made when appropriate.

essarily result in a protein having activity Y, those of ordinary skill in the art would expect that many of these conservative substitutions would result in a protein having the required activity. Further, amino acid substitutions outside of the two identified functional domains are unlikely to greatly affect activity Y. Thus, a correlation exists between the function of the claimed protein and the structure of the disclosed binding and catalytic domains. Consequently, there is information about which nucleic acids can vary from SEQ ID NO: 1 in the claimed genus of nucleic acids and still encode a polypeptide having activity Y. Based on the applicant's disclosure and the knowledge within the art, those of ordinary skill in the art would conclude that the applicant would have been in possession of the claimed genus of nucleic acids based on the disclosure of the single species of SEQ ID NO: 1.

Conclusion:

The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the scope of claim 2.